THE EFFECT OF GLUCOSE CONCENTRATIONS ON THE HEALING OF DIABETIC FOOT ULCERS IN SUBJECTS RECEIVING HYPERBARIC OXYGEN THERAPY

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CHAPTER I

INTRODUCTION

The diabetic foot ulcer is a common complication that develops in individuals with diabetes mellitus. It is estimated that up to 15% of individuals with diabetes will experience having a diabetic foot ulcer some time in their lifetime (1). Having a diabetic foot ulcer can ultimately lead to many changes in an individual's lifestyle. Some minor changes may include wearing special shoes designed for individuals suffering from foot ulcers or daily changing dressings on the ulcer. A major change that can occur in the lifestyle of an individual with a foot ulcer is amputation which has a devastating toll on a person.

Foot ulcers are common in people with diabetes mellitus. Twenty percent of hospital admissions for patients with diabetes are due to lower extremity problems (2). Many lower extremity amputations are performed due to non-healing foot ulcers. There are approximately 1,000,000 individuals in United States with diabetes that are suffering from lower extremity ulcers (2). Each year there are about 86,000 patients with diabetes that require lower extremity amputations due to diabetic ulceration (3). The single most common precursor for lower-extremity amputations is ulceration. It is estimated that 84% of lower extremity amputations in individuals with diabetes are caused by ulceration (4).

The two most common causes of diabetic foot ulcers are neuropathy and peripheral vascular disease (5). Individuals with poorly controlled diabetes develop these diseases (6). Neuropathy is nerve damage, usually in the lower extremities, that causes loss of feeling. With the loss of sensation in the feet, the individual can inflict trauma to the feet without knowing. New pressure points on the feet can also develop from changes in the individual's walking style due to muscle atrophy caused from neuropathy. Wounds and new pressure points can then lead to ulceration and infection.

Peripheral vascular disease due to diabetes causes decreased blood flow to the lower extremities. Blood flow is essential to deliver oxygen and nutrients to the peripheral tissues and to carry away waste products from the tissues. With decreased blood flow, tissues are unable to receive adequate oxygen and nutrients needed by the cells for proper wound healing. Gangrene, sometimes caused by an anaerobic bacteria, can develop with the absence of oxygen caused by peripheral vascular disease. The low concentrations of oxygen in the tissues allow the bacteria to survive and grow (4). Poor wound healing and the development of gangrene due to peripheral vascular disease can lead to stasis ulcers and possibly amputation (4).

There are many approaches for treating diabetic foot ulcers to prevent amputations. Using a multidisciplinary treatment approach increases the probability of healing. In a randomized study there was a 44 –85% decrease in ulcers and amputations in patients that took part in a multidisciplinary diabetic foot care program (7). Some treatments and preventive measures that were utilized included thorough foot risk assessments by a physician, callus and nail care, customized foot wear, wound care and debridement, and patient education from a multidisciplinary team with good knowledge of the foot (7). A relatively new treatment for the healing of diabetic foot ulcers is hyperbaric oxygen therapy (HBO). Most of all, good blood glucose control is an effective preventive measure for all diabetic complications (1).

Hyperbaric oxygen therapy can reduce the risk of amputation in people with diabetic foot ulcers (2,8). In one study, subjects that received hyperbaric oxygen for the treatment of a diabetic foot ulcer had a significantly lower occurrence of amputation compared to subjects that did not receive hyperbaric oxygen therapy (8).

Good glycemic control can decrease the risk of amputation in individuals with diabetic foot ulcers. Poor glycemic control is a significant predictor of the incidence of amputation (9). Studies have not been conducted to examine glycemic control of subjects with diabetes receiving hyperbaric oxygen therapy that resulted in successful wound healing or amputation.

The objective of this study is:

To determine if there is a significant difference in glucose concentrations of diabetic subjects receiving hyperbaric oxygen therapy that had successful wound healing and compared to those that had amputations.

Therefore the hypothesis of this study is:

Subjects with diabetes receiving hyperbaric oxygen therapy for the treatment of diabetic foot ulcers with successful wound healing will have better glucose concentrations compared to those that had amputations.

This study compares glucose concentrations to the success of healing of diabetic foot ulcers in subjects receiving hyperbaric oxygen therapy. The results of this study will be beneficial in identifying a possible adjunctive multidisciplinary approach for the treatment of diabetic foot ulcers and a preventative measure to reduce the risk of amputation.

CHAPTER II

REVIEW OF LITERATURE

Diabetes mellitus is a common disease that has a major impact on an individual's life. This disease is a precursor to many other diseases and complications. One of the complications that can change the quality of life for an individual with diabetes is a foot ulcer. Many interventions are utilized to prevent and treat diabetic foot ulcers such as good glycemic control, wearing proper footwear, debridement, vascular reconstruction, keeping weight off the foot, and hyperbaric oxygen therapy. If the diabetic foot ulcer is not cared for properly, the risk for an amputation increases (Table 1). Undergoing an amputation can be devastating for a person and drastically affects quality of life.

Using a multidisciplinary treatment approach increases the probability of healing. Good glycemic control is one approach that has been shown to improve the healing of ulcers and prevent further development of ulcers (6,9). Hyperbaric oxygen therapy is a relatively new method of treatment in the healing of diabetic foot ulcers and has been shown to increase the healing rate and decrease the risk of major amputation (2,8). The combination of glycemic control, regular wound care and hyperbaric oxygen therapy may be a good combination for the treatment of foot ulcers and prevention of amputation. This chapter will review diabetes, glycemic control, diabetic foot ulcers, treatments used for diabetic foot ulcers, wound healing, and hyperbaric oxygen therapy.

Diabetes and Glycemic Control

Diabetes mellitus is a major chronic metabolic disorder that has been diagnosed in approximately 5-6% of the population of the United States. This accounts for about 17 million people, and over 5 million of these people are unaware that they have this disease (3). Each year about 800,000 people are diagnosed with this life long condition (3). Minority groups including African-Americans, Mexican Americans, and Native Americans are the most frequently affected by diabetes (10). The National Center for Health Statistics estimated that 64,751 deaths in 1999 were caused by diabetes in the United States. This is a rate of 13.6 deaths per 100,000 deaths (11). This mortality estimate is thought to be underestimated because this estimate only accounts for people with their primary diagnosis as diabetes. Taking into account that diabetes is a precursor of many other long term life threatening diseases such as nephropathy, neuropathy, retinopathy, cardiovascular disease, and peripheral vascular disease the estimated number of deaths is 193,140 (3). Diabetes increases the risk of heart disease and stoke in adults 2-4 times higher than adults without diabetes (3).

The definition of diabetes mellitus is the absence of insulin, insufficient amount of insulin, or insulin not properly used by target tissues (12). Diabetes mellitus is divided into two etiopathogenetic categories which are type 1 and type 2 diabetes. This metabolic disease is characterized by hyperglycemia and some of the symptoms that are indicators of hyperglycemia are polyuria, polydispia, blurred vision, and weight loss. Ketoacidosis that may occur in some individuals with diabetes, is a dangerous, life threatening effect of hyperglycemia (13).

Type 1 diabetes can be immune-mediated or idiopathic. Immune-mediated diabetes is developed from an autoimmune destruction and malfunction of beta cells in the pancreas. The cause of the destruction of beta cells may be related to genetic characteristics or to environmental factors that have not been clearly defined. The destruction of beta cells stops the production of insulin and the pancreas ultimately is unable to regulate glucose levels in the blood. The rate of destruction of beta cells in the pancreas is different in each person. The rate of destruction is usually faster in infants and children and slower in adults. The first indication of type 1 diabetes in many children and adolescents is ketoacidosis. Others may experience mild hyperglycemia and then develop severe hyperglycemia or ketoacidosis when infection or stress is present. For many adults, beta cell function may remain adequate to prevent ketoacidosis from occurring for a long period. Eventually, individuals with type 1 diabetes become dependent on insulin replacement therapy for survival (13).

Type 1 diabetes can also be idiopathic. Individuals with this kind of type 1 diabetes have no autoimmune destruction present but have little or no insulin production and are likely to develop ketoacidosis. The level of insulin available to the body changes and the requirement for insulin replacement therapy may come and go. Only a minority of individuals have this condition and most that do are of African or Asian descent. Idiopathic diabetes is inherited and there is no evidence of destruction of beta cells by an autoimmune reaction (13).

Type 2 diabetes occurs in individuals who develop insulin resistance and may progress to insulin deficiency. Years may pass without diabetes being diagnosed because hyperglycemia develops slowly in the beginning and the signs of hyperglycemia may not be strong enough for the individual to notice. Many individuals with type 2 diabetes do not require the use of insulin replacement therapy to survive, but some may require insulin after several years with diabetes. This type of diabetes is not caused by autoimmune destruction of beta cells. The causes of type 2 diabetes have not been clearly defined but there is genetic a link for this disease. Some of the characteristics of individuals with type 2 diabetes include being overweight or obese with increased percentage of body fat in the abdominal area and physical inactivity (13). Type 2 diabetes may be also associated with hyperlipidemia and polycystic ovary syndrome.

Glycemic control is the primary treatment goal for individuals with diabetes. Glycemic control can be defined as maintaining blood glucose levels within an acceptable range. The normal range for fasting blood glucose levels is <110mg/dL. Those with impaired glucose tolerance (pre-diabetes) have fasting blood glucose levels of $\geq$110 and <126mg/dL or a random concentration of $\geq$140 and <200mg/dL and individuals with fasting blood glucose levels >126mg/dL have diabetes (11). Self-monitoring of blood glucose is a method to monitor glycemic control. A person with diabetes can work with a dietitian and other healthcare professionals to determine the best behaviors for achieving the ideal glucose range. By self-monitoring their blood glucose and by trying various combinations of diet, exercise and medication, the individual and healthcare provider can determine the best combination for optimal blood glucose control.

The Diabetes Control and Complications Trial clearly demonstrated that good glycemic control reduced the incidence and prevalence of retinopathy, nephropathy, and neuropathy in people with type 1 diabetes (6). Retinopathy was 60% less prevalent in subjects with intensive self-monitoring of blood glucose and insulin treatment compared to the control group. In the study, subjects who took part in intensive insulin therapy had a reduction in progression in renal disease as evidenced by a 39% reduction in incidence of microalbuminuria and a 54% reduction in incidence of macroalbuminuria. This study also reported that those who achieved near normal glycemic control had a 69% reduction in subclinical neuropathy and a 57% reduction in clinical neuropathy compared to control subjects (6). Neuropathy is one of the leading causes of foot ulcers and sores (5).

Hemoglobin A1c (HbA1c) is an accurate method to assess glycemic control because is reflects glycemia over the past 6 to 12 weeks. Hemoglobin A1C can be quantified to measure the amount of hemoglobin that is glycosylated. Individuals with good glycemic control have an HbA1c of <6%. The goal for individuals with diabetes is to have HbA1c <7% and those that need intervention have HbA1c >8% (11).

Individuals with elevated glycosylated hemoglobin concentrations have a higher incidence of developing sores or ulcers compared to individuals with near normal glycosylated hemoglobin concentrations. Persons taking insulin a greater risk of developing sores and ulcers compared to those who do not take insulin (9). Some of the other independent risk factors for developing sores or ulcers are long duration of diabetes, proteinuria, and low diastolic blood pressure. All of these risk factors with the addition of being male are also predictors for amputation (9).

Poorly controlled diabetes is a precursor of many long-term complications and is the leading cause of blindness, end stage renal disease (ESRD) and amputation (14). Retinopathy caused by diabetes is the leading cause for blindness in people aged 20-74 years (10). In 1996, 42% of new cases of ESRD were in patients with diabetes (15). The U.S. National Hospital Discharge survey showed that 51% of nontraumatic lower limb amputations were performed on individuals with diabetes from 1989-1991. Amputations were performed to remove toes (40%), foot and ankle (15%), and limbs below the knee (25%) or above the knee (20%) (16).

Good glycemic control can reduce the risk of many life long diseases and reduce the incidence of foot sores and ulcers (6). The risk of amputation would decrease also. Reducing in the risk for these diseases could prolong and provide a better quality of life. For individuals with diabetes, good glycemic control should be the primary goal for the control of the disease and their health. Despite the evidence that good glycemic control is beneficial for people with diabetes, many with this disease have poor glucose control because they are limited in their access to consistent and continuous health care, insulin therapy and other therapies available for the management of diabetes (17).

Diabetic Foot Ulcers

Diabetic foot ulcers are a problem of great concern that can change an individual's quality of life and health. Foot ulcers are one of the most common long-term complications of diabetes. It is estimated that 15% of all people with diabetes will be affected with a foot ulcer in their lifetime and of this 15%, males aged 45-64 years old are at the highest risk for developing a foot ulcer (16). In this era, there have been many changes in treatment approaches to save the diabetic foot from infection, gangrene and amputation. Currently there are no widely accepted guidelines for preventing, assessing and treating the diabetic foot ulcer. To date, treatment has been based on consensus and scientific methodology to determine the best approach (18). With today's understanding of the pathophysiology of the diabetic foot, treatment can be customized to the individual to meet their needs.

Diabetic foot ulcers are defined as local defects to the surface of skin caused by the sloughing of necrotic inflammatory tissue (19). The most common location of a foot ulcer is on the plantar region of the foot (20). Other common areas that foot ulcers form are on the top of toe joints (Appendix A). The severity of the ulcer is based on the depth, presence of infection and peripheral vascular disease. Diabetic foot ulcers range from superficial to deep ulcers to the tendon, bone, or joint. Infections also vary in severity. In severe ulcers, infection, abscess, osteomylitis, ischemia and gangrene can develop (4).

The wound healing process includes four phases that overlap. They are the hemostatic phase, the inflammatory phase, the proliferation, maturation or connective tissue phase and the remodeling or epithelial phase. The hemostatic phase starts as soon as the wound occurs wherein platelets and leukocytes initiate blood coagulation and the beginning of the inflammatory phase. During the inflammatory phase, leukocytes ingest bacteria and debris in the wound and macrophages begin the connective tissue phase by releasing growth factors to stimulate the synthesis of capillaries to vascularize the tissue. The connective tissue phase promotes closing the wound by fibroblasts producing collagen and begins the epithelial phase by myofibrils facilitating epidermal coverage. The epithelial phase is the last phase in wound healing in which the epithelial cells begin covering the wound. The wound is considered to be healed only when the tissue strength is normal and is across the entire wound (21).

One system that is used to describe the severity of wounds is the red-yellow-black system (22). It uses color to identify the stage the wound is in during the healing process. Red wounds indicate that it is in the inflammatory or the proliferation/ maturation phase of wound healing. Yellow wounds indicate that the wound is not ready to heal due to infection or the wound contains fibrinous slough. Black wounds are not in the healing phase due to necrotic tissue (22).

Another system used to describe the severity of foot ulcers is the Wagner scale (4). It is one of the most commonly cited diabetic wound classification systems used. This system has six grades (0-5) and is based on the depth of the wound. A higher grade indicates the wound is deeper and more severe. Grade 0 represents skin that is intact, grade 1 indicates a superficial ulcer, grade 2 is a deep ulcer to the tendon, bone or joint, grade 3 is a deep ulcer with abscess or osteomyelitis, grade 4 is forefoot gangrene and grade 5 is whole foot gangrene (4).

Peripheral neuropathy and peripheral vascular disease are two diseases that develop with poorly controlled diabetes and are the leading causes of foot ulcers (5). These conditions cause changes to the lower extremities that increase the risk of developing foot ulcers. The severity of the ulcer also depends on the amount of blood that is available to the tissue. The presence of peripheral vascular disease can greatly impact the severity of the ulcer by depriving the tissue of oxygen needed to heal the tissue and fight infection (4).

Peripheral neuropathy is nerve dysfunction that affects sensation of the lower extremities, especially in the foot. This disease causes functional disturbances and pathologic changes in the peripheral nervous system. The nerves in the lower limbs are affected and often the autonomic nerves are also affected. The pathology of this disease is segmental demyelination of the peripheral nerves. Without a myelin sheath around the peripheral nerves, transmissions of impulses are slowed and damage is caused to the nerves (19). This disease is associated with an 8 to 18 fold higher risk of ulceration and a 2 to 15 fold higher risk of amputation (1). The prevalence of this condition increases with age, duration of diabetes, presence of microvascular complications, and poor glycemic control (23). It affects up to 50% of the people who have had diabetes for more than fifteen years (24).

Peripheral neuropathy is the cause of several changes in the lower extremities. One change is loss of sensation which leads to extensive damage to the foot because the sensations that signal an individual to protect their feet (such as pain, pressure, and temperature) are lost (1). Individuals with the loss of sensation can cause trauma to the foot without knowing it. When trauma is unattended, it ultimately leads to infection and ulceration.

Atrophy of the intrinsic muscles is another change that can occur with peripheral neuropathy. This results in flexion deformity. This condition causes limitations to the full movement of the foot and leads to changes in an individual's gait. Changes in gait increase pressure under the metatarsal heads and the toes, increasing the risk for ulcer development in these areas (1).

Lastly, peripheral neuropathy can also decrease perspiration in the foot leading to dry skin that causes cracks and fissures in the feet (5). All these changes caused by peripheral neuropathy increase the risk of developing ulcers and delay the healing of ulcers that already exist.

Peripheral vascular disease (PVD), on the other hand, is atherosclerosis of the peripheral blood vessels. This disease is identified by intermittent claudication and/or the absence of peripheral pulse or blood flow in the lower limbs and feet (25). Individuals with diabetes are 2-3 times more likely to develop this PVD than the general population (26) and the prevalence of this disease increases with age and the duration of diabetes (25). Only 5-7% of ulcers are due to peripheral vascular disease and is not a leading cause of foot ulcers (27).

Although peripheral vascular disease may not be the leading cause of the development of foot ulcers, it has profound effects on the progression of healing. Due to decreased blood perfusion in the lower limbs, the risk for infection, poor healing of sores and ulcers, and gangrene increases. If the ulceration is unable to heal, it can ultimately lead to amputation. Almost half of amputations are attributed to peripheral vascular disease (28). When an individual must undergo an amputation there is a 28-51% chance that within five years the individual will require a second amputation and unfortunately, three years after an amputation the survival rate is less than 50% (25).

Peripheral vascular disease decreases oxygen supply to the tissues in the lower extremities. Peripheral vascular disease affects the femoral and iliac arteries in all individuals but in diabetics it is more likely to also have involvement with the peroneal and tibial vessels (1). Vessel occlusion that occurs with this disease inhibits adequate blood circulation to the lower legs and feet. With decreased arterial circulation in the lower extremities, there is inadequate cutaneous perfusion of oxygen (16). Cutaneous circulation indicates the amount of oxygen diffusion across the skin which is measured by using transcutaneous oxygen tension (TcPO2) values. Values of TcPO2 can predict the potential for the healing of lower extremity wounds. A TcPO2 value of < 20 mmHg is associated with poor healing while 20-40 mmHg is associated with intermediate healing and values >40 mmHg are associated with a high likelihood of healing (29).

The amount of oxygen saturation of the tissues is one determining factor in healing. Fibroblasts synthesize collagen only when there is adequate oxygen in the tissues. Peripheral vascular disease does not allow for adequate oxygen saturation of the tissues. Hypoxia caused by peripheral vascular disease prevents fibroblasts from synthesizing collagen to initiate wound healing (30).

Other factors along with adequate oxygen saturation of tissue that should be considered in the wound healing process are nutritional status and delivery of nutrients to the tissues. The wound healing process is dependent on the presence of oxygen and nutrients in each phase. During all phases of wound healing, blood flow and good nutritional status are essential. Good blood flow enables the delivery of oxygen and all the needed nutrients and factors that promote the healing process. The delivery of glucose to the wound serves as the primary source of energy and promotes phagocytic activity of the lymphocytes (21). The presence of hyperglycemia however is a risk factor for poorer wound healing due to the loss of other nutrients from glycosuria (31). The delivery of protein to the wound is essential to assist in cellular multiplication, fibroblastic proliferation and collagen synthesis. Collagen synthesis requires adequate amounts of vitamin A, C, B-complex vitamins and copper (21).

Amino acids are the building blocks for collagen synthesis. Vitamins A, B (thiamin), C, E, and K; the minerals calcium, copper, and zinc are all essential for wound healing to occur. Vitamin A provides a defense system against infections and complications that may occur. Vitamin K protects against infection by promoting blood clotting and preventing prolonged bleeding. Vitamin C is an essential cofactor for the synthesis of collagen and thiamin is used to strengthen collagen. With the absence of vitamin E the synthesis of collagen may be impaired and slow down the process of wound healing. Calcium is a cofactor during collagen remodeling and copper is needed by collagen to enhance scar strength. Zinc is essential for the synthesis of nucleic acid that is necessary for many enzymatic reactions to occur during wound healing (21).

Adequate intake of food or other nutritional interventions (i.e. tube feeding, supplements) are essential for proper wound healing. The wound needs good nutrition, such as adequate calories, protein, vitamin and minerals, and fluids, to make wound healing possible. Any element that causes malnutrition will retard the wound healing process (21). Many times, the stage or severity of the wound is related to nutritional deficits, especially inadequate protein intake reflected by low serum albumin levels (32). A depressed level of serum albumin increases the risk of poor wound healing by threefold with each gram decrease in serum albumin (21). For individuals with wounds, the recommended amount of protein needed for the wound to heal is 1.2-1.5g/kg (32).

Other than protein, the vitamins and minerals discussed previously are needed to assist in the wound healing process. For individuals that do not receive adequate vitamins and minerals in their diet should take a multivitamin daily to aid in the wound healing process (32). Individuals that most likely need supplementation are those that have lost <10% of lean body mass. The weight loss is an indicator that the individual most likely has not received proper nutrition.

Nutrition plays an important role in wound healing. In a study, individuals with chronic ulcers had significantly lower levels of serum Vitamin A, Vitamin E, zinc, and carotenes compared to healthy individuals in the Boston area. This study concluded that nutritional deficiencies of these nutrients may have a negative effect on wound healing (33).

Steps that the individual can take to assist in the healing of a diabetic foot ulcer are keeping weight and stress off the foot, wearing special foot wear, debriding the wound, maintaining a moist environment with dressings, managing infection, undergoing vascular surgery, and controlling diabetes (34).

Keeping stress off the foot, also called off-loading, can be done in several ways. One way to keep stress of the foot is by a total contact cast (TCC). The TCC is applied to the foot to keep pressure off wounds on the planter part of the foot. TCC is used only in individuals who do no have any infection or ischemic wounds. Other treatments for off-loading are bed rest, surgical shoes, half shoes, sandals, and felted foam dressings. Bed rest is the only intervention that does not require the use of crutches. The top priority for the individual is to keep the foot off the ground as much as possible. Continuance of these interventions for approximately two weeks after the ulcer heals is recommended to give the wound time to mature and prevent the recurrence of the ulcer (18).

Footwear that is customized to fit the individual properly can reduce pressure, prevent trauma, and reduce the formation of calluses and ulcers in people with diabetes (1). Special footwear can also protect an existing ulcer from further damage. Some principles for choosing the right footwear are summarized by Tovey (35). One principle is to choose a shoe that is the right size, reduces pressure to the plantar area of the foot, reduces shock, and forms around any deformities of the foot. The shoe should be longer than the top of the longest toe by at least 3/8 inch to provide enough room. The heel of the shoe should fit comfortably without any rubbing on the heel. For individuals with edema or deformities of the foot, shoes with laces are best to allow for adjustments to form around the foot properly. Following these principles, prevents development of ulcers in high-risk people.

Debridement of dead tissue from the wound area assists in wound healing. A healthcare provider removes the tissue with a scalpel and forceps. If the wound is not infected, debridement can be done on an outpatient basis. If the wound is infected, most debridements will occur in-patient. This process removes all necrotic tissue and drains the wound to prevent any pooling of pus that might occur. Sharp debridement is a safer method of debridement compared to whirlpool or other hydrotherapies. It reduces the risk of developing infections or burns that hydrotherapies may cause (18).

Keeping the wound in a moist environment is important in the healing process. Dressings are used to maintain and provide the wound with moisture. Dressings also are used to prevent infection and prevent further trauma to the wound. The type of dressing used is important to ensure it will provide the wound with the appropriate environment for healing to occur. Guidelines for choosing dressings are the wound type, presence of exudate, condition of surrounding skin, likelihood of reinjury, and cost. Dressings can be a low cost treatment because the individual or a caregiver can change the dressing at home. Dressings should be used with off-loading and debridement to produce the best results for wound healing (18).

Management of infection can assist in wound healing and help prevent the possibility of amputation. Identifying an infected wound is based on clinical evidence rather than microbiological evidence. All wounds have potentially pathogenic organisms present but the wound may not be infected. Clinical criteria such as the presence of pus or two or more signs of inflammation are signs that infection is present. When infection is identified the use of antimicrobial therapy is put in place (18).

Vascular reconstruction is used in patients with poor circulation in the foot. No infection can be present to perform this surgery. This surgery is able to reconstruct the vessels in the foot to provide better circulation which will then restore arterial flow and pulse to the foot (18). Vascular reconstruction has been shown to heal wounds quickly and reduce amputations (36).

Treating the diabetic foot wound has several benefits to the individual and reduces costs (18). Treating a diabetic foot wound improves function and quality of life. Treatment allows the individual to return to ambulating, relieves health care providers or caregivers from having to change dressings, and allows the individual to participate in normal daily activities. Controlling infection maintains the individual in good health and can ultimately prevent the occurrence of amputation. Treating the wound costs less and reduces cost by avoiding the cost of amputation and hospitalization (18).

Hyperbaric Oxygen Therapy (HBO)

The use of hyperbaric oxygen (HBO) therapy is in it's beginning in the medical field. It has been used for a little over forty years (37). The first clinical use of the hyperbaric chamber was in 1955 by Churchill-Davidson and was used to resemble the effects of radiation therapy in cancer patients. Soon after, in 1956, Professor Ite Boerema at the University Hospital in Amsterdam performed vascular and cardiac surgery under hyperbaric conditions in a chamber to prolong the patient's tolerance to circulatory arrest (38). There is skepticism among many medical professionals of what diseases or conditions it can treat. The main concern many medical professionals have is that there has not been sufficient scientific validation of the efficacy or safety of this treatment (37).

Currently, there are a limited number of conditions approved to be treated by hyperbaric oxygen therapy. One condition is the enhancement of healing in selected problem wounds, such as diabetic foot ulcers and venous ulcers. Other disorders approved for treatment with hyperbaric oxygen therapy are: decompression sickness, gas embolism, carbon monoxide and cyanide poisoning, gas gangrene, osteomyelitis, sternal wound infections, radiation injury to tissue, blood loss anemia, crush injury and other traumatic peripheral ischemias, skin grafts and flaps, management of fungal disease, treatment of thermal burns, and pelvic radiation necrosis and radiation cyctitis (38). All of the conditions listed have a common pathophysiology of local or focal hypoxia and are the only approved conditions to be treated with HBO (2). HBO is used to treat other conditions that are not approved, such as rheumatoid arthritis, cirrhosis, and gastoduodenal ulcers. The effectiveness of HBO in the treatment of these conditions remain unproven (37).

The use of HBO to treat diabetic foot ulcers is not recommended for all individuals with this condition (2). Those with ulcers that are not severe (stage 1 or 2 on the Wagner scale) are first treated with more traditional forms of therapy. Some of the traditional forms of therapy for foot ulcers include doing regular foot exams, maintaining glycemic control, wearing special footwear, and keeping weight/pressure off the wound (1). Individuals that would be considered for HBO include patients with class 3, 4, or 5 Wagner scale ulcers and those with inadequate arterial flow in the extremities (2).

Hyperbaric oxygen therapy is administered in a mono- or multiplace chamber for approximately 1-2 hours a day, 5-6 days a week. The average number or treatments for optimal wound healing is 30-40 treatments (37). A monoplace chamber is made to accommodate only one individual and is used primarily for patients with chronic medical conditions. This chamber provides a100% oxygen environment under increased pressure. A multiplace chamber can hold several individuals at one time and is usually used for patients with acute medical problems and critically ill patients. In this chamber an attendant is always present inside the chamber in case any complications arise. This chamber provides increased pressure, but the environment does not provide

100% oxygen. Patients are required to wear a mask, tight fitting hood or have an endotracheal tube to provide the patient with 100% oxygen (37).

The physiologic effects of hyperbaric oxygen therapy on the body assist in the healing process of the diabetic foot ulcer. The oxygen level and atmospheric pressure while in the hyperbaric chamber play a part in causing physiological changes in the body (39). In the normal environment, the composition of the air is only 21% oxygen (38). HBO provides the patient with almost five times the amount of oxygen than normal environment. While breathing in 100% oxygen the patient is also under increased atmospheric pressure. The pressure equivalent of 3 atmospheres (ATA), which is like being under 66 ft of sea water, is used in the hyperbaric chamber (40). Increasing the pressure above this level can be harmful by inducing the toxic effects of oxygen such as grand mal seizures and damage to the lung tissue (38).

Under increased pressure and breathing 100% oxygen, the oxygen content of the blood increases. Hemoglobin in normal conditions is 97% saturated with the oxygen breathed in. By changing the air to 100% oxygen, an increase of 3% of hemoglobin-delivered oxygen will occur and the rest of the oxygen will be dissolved in the plasma. By increasing the atmospheric pressure, the oxygen dissolved in the plasma will increase by 2.3 vol%. Thus at 3 ATA, more than 6 vol% of the plasma is saturated with oxygen (41). This increase of oxygen content of the plasma is equal to ten to fifteen times more than the normal saturation level of the plasma in a normal environment (2).

The increased pressure also has an effect on the volume of the gas bubbles in the blood. Boyle's law explains the reason for change in the volume of gas bubbles in the blood while in the hyperbaric chamber. The basic theory of Boyle's law is that at a constant temperature and mass, the volume of a perfect gas varies inversely with pressure (19). Thus, as the pressure increases, the size of the gas bubble decreases. At 3 ATA the bubble volume of a gas is decreased by two thirds. This allows the intravascular bubbles that cause obstruction to move to smaller vessels which then reduces damage to extravascular tissue (37). As gas bubbles become microscopically small and reach thousands of dynes per square centimeter, better circulation to areas with poor circulation, such as the foot, is made possible (38). Increasing the circulation in the foot and increasing the oxygen content of the blood allows for greater re-oxygenation of ulcerated tissue to assist in wound healing (37).

Hyperbaric oxygen therapy increases the oxygen saturation of tissue. Increased oxygen saturation of the tissue can assist in healing of a diabetic foot ulcer. Fibroblasts synthesize collagen only when there is adequate oxygen in the tissues. The deposition of collagen and it's ability to condense is highly dependent of the amount of oxygen available to the tissue. With well-oxygenated and hydrated tissues, epithelial cells can move and replicate to promote wound healing (42).

Hyperbaric oxygen therapy is effective in healing diabetic foot ulcers and preventing amputations. The results of a randomized study performed by Faglia et al. (8) showed that hyperbaric oxygen therapy was successful in decreasing the number of amputations in subjects receiving HBO compared to those who did not receive HBO (8). In this study, 35 subjects underwent hyperbaric oxygen therapy for a diabetic foot ulcer and 33 subjects did not. Three subjects (8.6%) in the treatment group underwent amputation and 11 subjects (33.3%) in the nontreatment group underwent amputation. The difference in the amputation rate between the groups was found to be statistically significant ($p=0.016$).

Baroni et al. (43) reported success in decreasing the rate of amputations in patients receiving hyperbaric oxygen therapy for the diabetic foot ulcer. In this study, 18 subjects were in the treatment group (received HBO therapy) and 10 were in the nontreatment group (did not receive HBO therapy). Two subjects in the treatment group and nine subjects in the nontreatment group did not heal. The rate of amputation in the treatment group was 12.5%, whereas the amputation rate in the nontreatment group was 40% which was statistically significant at ($p<0.001$). Sixteen patients in treatment group healed and were discharged in 62 days compared to nine patients in the nontreated group that did not heal in 82 days.

Hyperbaric oxygen therapy is a useful treatment in reducing the risk of amputations in subjects with diabetic ulcers. The results of these studies and the physiologically effects of hyperbaric oxygen therapy on the body give good supportive evidence that the use of hyperbaric oxygen therapy is a beneficial form of adjunctive treatment for the healing of diabetic foot ulcers and a preventive measure to amputation.

Understanding the pathophysiology and care needed for diabetic foot ulcers are useful in providing an individual with proper care for their condition. This understanding can also provide healthcare providers with more direction in using new treatments that may enhance those already in place. With further understanding of wound healing and the use of effective treatments, the severity of ulcers and risk of amputations can be reduced and provide individuals with diabetes a better quality of life and health.

In summary, the maintenance of good glycemic control and the use of hyperbaric oxygen therapy may be a good interdisciplinary approach in assisting in the healing of diabetic foot ulcers. There are no present studies that investigate the effect of the combination of good glycemic control and hyperbaric oxygen therapy on the healing of diabetic foot ulcers. Information provided from the literature review leads to the hypothesis of this study: Subjects with diabetes receiving hyperbaric oxygen therapy for the treatment of diabetic foot ulcers with successful wound healing will have better glucose concentrations compared to those that had amputations.

Table 1. Risk factors for lower extremity amputations of the diabetic foot
Peripheral neuropathy- loss of sensation in the foot
Peripheral vascular disease- poor circulation
High pressure points formed from foot deformity and callus formation
Autonomic neuropathy- decrease sweating and dry, fissured skin
Obesity
Impaired vision
Poor glycemic control- causes impaired wound healing
Poor foot wear- causes skin breakdown and increases pressure points
History of foot ulcers and lower extremity amputation
Armstrong DG & Lavery LA, American Family Physician, 1998.

CHAPTER III

METHODOLOGY

This study is a retrospective hospital based study that was approved by the Integris Baptist Hospital Institutional Review Board and the Oklahoma State University Institutional Review Board (Appendix B & C). Data were collected from a retrospective review of consecutive medical charts in the baromedical unit at Integris Baptist Medical Center in Oklahoma City, Oklahoma. Fifty-eight charts of patients admitted in 1997 to 2001 for hyperbaric oxygen therapy were reviewed. Thirty-five of the charts reviewed were not included in the study due because the patients did not meet the inclusion criteria because the chart did not have adequate information.

Subjects

The subjects used in this study were patients with diabetes that had received outpatient hyperbaric oxygen therapy for diabetic ulcers at Integris Baptist Medical Center in Oklahoma City, Oklahoma from July 1997 to April 2001. All subjects received the hyperbaric oxygen therapy in the morning. Twenty-three subjects were included in this study. To be included in this study, subjects had to have the diagnosis of type 1 or type 2 diabetes with a diabetic foot ulcer, had undergone outpatient HBO therapy for the treatment of the diabetic foot ulcer and were compliant with HBO treatments. Being compliant with HBO therapy was defined as not missing treatments and completing all treatments that the physician ordered for the patient. Lastly, the subjects had to be free of any other infections.

Data Collection

Medical charts from Integris Baptist Medical Center between July 1997 and April 2001 were reviewed starting from the most recent patients that received HBO for the treatment of a diabetic foot ulcer. Sampling was consecutive. Patient confidentiality was assured by not identifying the patient in any way on the data collection sheet. The patient's name, social security number, medical chart number, address, phone number, or any other identifying data was not recorded. Instead, each patient's chart reviewed was given an identification number between one and twenty-three. The patient age, sex, diagnoses, glucose levels before HBO treatments, location of ulcer, color stages of ulcer (initial and throughout treatment), dates of treatments, the number of treatments, and amputations were collected. The diagnosis of type 1 or type 2 diabetes was not included in the medical charts. Only the diagnosis of diabetes was in the medical charts. These data were recorded onto a data collection sheet to be analyzed for later analysis (Appendix D).

Whole blood glucose levels (random, not fasting) before HBO treatment were used to determine the patient's glucose concentrations during the time of the treatment. The nurse present took and recorded each subject's whole blood glucose level with the glucometer in the unit. Average blood glucose levels throughout HBO treatment were estimated by using the Excel program. This provided a good estimate of the average blood glucose level before each HBO treatment. The range of blood glucose levels before HBO therapy were also recorded to determine if blood glucose levels were stable.

In order to determine healing of the ulcer, the stage of the wound was evaluated and recorded in the medical chart by a nurse. The colors red, yellow, and black were used. Red indicated the wound was in the healing stage (21). Yellow indicated the wound was not ready for healing due to infection or fibrinous slough. Black indicated necrotic non-healing tissue. The number of treatments per color stage was also recorded. This would indicate how long the healing process took in each stage of color.

Individuals that required an amputation were recorded in the medical chart. On the last HBO treatment given to the patient, the date for surgery to amputate was recorded. This indicated which patients required an amputation.

Analysis of Data

The Excel program was used to compute means, standard deviations and percents of the descriptive results of two groups. The subjects were grouped according to whether the individual received an amputation. Means and standard deviations for age, number of hyperbaric oxygen therapy treatments in each stage (black, yellow and red), total number of hyperbaric oxygen therapy treatments and glucose concentrations throughout HBO and in each stage (black, yellow and red) were computed for each group. Percents were computed for the ration of individuals with specific diagnoses. T-tests were computed to determine if there was a significant difference between the groups in glucose concentrations throughout the treatments, in each stage (black, yellow and red), and minimum and maximum glucose concentrations. The t-test was also used to determine if there was a significant difference in the number of HBO treatments the groups received.

Due to the lack of objective data in the patient's medical charts, each group is described in detail to give a clearer picture of the subjects in each group. The description includes the progression of wound healing or non-wound healing of each subject.

CHAPTER IV

RESULTS

Twenty-three subjects with diabetic foot ulcers were included in this study by a retrospective review of medical charts in the baromedical unit at Integris Baptist Medical Center in Oklahoma City, Oklahoma. The study included 15 males and 8 females. All subjects were diagnosed with diabetes and underwent hyperbaric oxygen therapy (HBO) for the treatment of a diabetic foot ulcer. Most (73.9%) of the subjects in this study were diagnosed with peripheral vascular disease which is identified as a risk factor for the development of diabetic foot ucers. Other diagnoses included heart disease (69.6%), hypertension (73.9%), cancer (8.7%), COPD (13.0%), kidney disease (13.0%), cellulitis (4.3%), and anemia (4.3%).

Of the thirteen subjects that did not require an amputation, 9 were male and 4 were female. The average age of this group was 61.4 $\pm$ 9.8 years and they had an average of 20.4$\pm$4.1 HBO treatments. The average glucose levels of this group in the wound healing stages of red, yellow and black were 174.9 $\pm$ 55.0 mg/dL, 178.5 $\pm$ 58.3 mg/dL, and 200.0 $\pm$ 115.8 mg/dL, respectively (Table 1 and Table 2).

Two subjects in non-amputated group began HBO treatment in the red stage of wound healing (Figure 1). One of the subjects that began in the red stage remained red throughout his 20 treatments and the other subject that began in the red stage declined to the yellow stage after three treatments. The wound then advanced to the red stage again after ten treatments and was able to heal after eight more treatments.

Nine subjects in the non-amputated group began HBO treatment in the yellow stage of wound healing (Figure 1). Eight of the nine subjects that began treatment in the yellow stage of wound healing advanced to the red stage and were able to heal. One subject that began in the yellow stage of healing declined to the black stage and received four treatments in this stage. This subject was able to advance to the red stage of wound healing and was able to heal.

Two subjects in this group began HBO in the black stage. They were both able to advance to the yellow stage and finally to the red stage of wound healing (Figure 1).

Of the ten subjects in this study that required an amputation, 6 were male and 4 were female. The average age of this group was 64.6 ± 8.7 years and had an average of 16.3 ± 7.1 HBO treatments. The average glucose levels in the red, yellow and black stages were 198.0 ± 0.0 mg/dL, 169.9 ± 40.7mg/dL, and 183.2 ± 34.3 mg/dL, respectively (Table 1 and Table 2).

Only one subject in this group began HBO in the red stage of wound healing (Figure 2). This subject regressed throughout the treatment. Ultimately, the ulcer worsened to the extent the physician ordered an amputation.

Three subjects in this group began HBO in the yellow stage of wound healing (Figure 2). One subject worsened to black and received one treatment and then advanced back to the yellow stage. After six treatments in the yellow stage the physician ordered an amputation. Two of the subjects that began HBO in the yellow stage of wound healing degenerated to the black stage and did not heal which ultimately resulted in amputations.

Six subjects in this group began HBO in the black stage of wound healing (Figure 2). Four subjects that began treatment in the black stage did not improve and required an amputation. One subject that began treatment in the black stage advanced to the yellow stage and received eight treatments in the yellow stage. The physician ordered an amputation after those treatments. Lastly, one subject that began treatment in the black stage of healing advanced to the yellow stage and received six treatments. This subject then declined to the black stage again and received two more treatments before amputation.

T-tests were performed to determine if there were significant differences between the groups (non-amputated and amputated). The significance level of $p=0.005$ was used for all of the t-tests. Blood glucose concentrations from each group in stages of black and yellow were compared. The results were as follows: black $p=0.652237$ and yellow $p= 0.734594$. The t-test results showed there was no significant difference in the glucose levels between the groups in each wound healing stage. A t-test in the red stage of healing was unable to be computed because only one subject in the amputated group was in the red stage. The t-test for overall glucose levels between the groups was $p=0.987601$. This indicates that there was no significance in glucose concentrations throughout the HBO treatments. Minimum and maximum glucose concentrations were compared. The t-test results were p=0.815054 (minimum) and p=0.712534 (maximum). The t-test determined that there was no significance between the group's minimum and maximum glucose concentrations.

T-test were also used to determine if there was a significant difference in the age, number of HBO treatments each group received, the number of diagnoses between the groups. The result of the t-test showed there was no significant difference in age (p=0.414658), number of HBO treatments (p=0.967981) or number of diagnoses (0.691848) between the amputated group and the healed group.

Table 1. Description of subjects in this study		
	Non-amputated n=13	Amputated n=10
Age (years)	61.4 ± 9.8	64.6 ± 8.7
Sex		
Male	9	6
Female	4	4
Diagnosis *(no. of subjects with each diagnosis)*		
Diabetes mellitus	13	10
Heart disease	8	8
Hypertension	10	6
Peripheral vascular disease	9	7
Cancer	1	1
COPD	2	1
Kidney disease	3	0
Cellulitis	0	1
CVA	1	2
Anemia	0	1
Total number of diagnoses	4.0 ± 1.4	3.7 ± 1.0

Table 2. Comparison of number of treatments and glucose levels by wound healing stages and whether patient was healed or amputated.

Wound Stage	Number of treatments ± SD		Glucose level ± SD (mg/dL)		Minimum glucose level ±SD (mg/dL)		Maximum glucose level ± SD (mg/dL)	
	Healed	Amputated	Healed	Amputated	Healed	Amputated	Healed	Amputated
All	20.4±4.1	16.3±7.1	178.9±61.3	178.8±35.7	126.8±59.2	123.1±37.5	240.2±78.4	232.0±61.0
Black	1.0±2.2	8.9±9.6	200.0±115.8	183.2±34.3	146.0±99.2	132.8±32.3	254.3±128	249.1±69.6
Yellow	9.6±4.8	5.5±5.2	178.5±58.3	169.4±40.7	112.2±45.0	101.7±40.1	254.0±71.3	215.1±40.7
Red	9.0±5.8	0.9±2.8	174.9±55.0	198.0±0.0	134.9±61.9	142.0±0.0	222.4±74.6	274.0±0.0

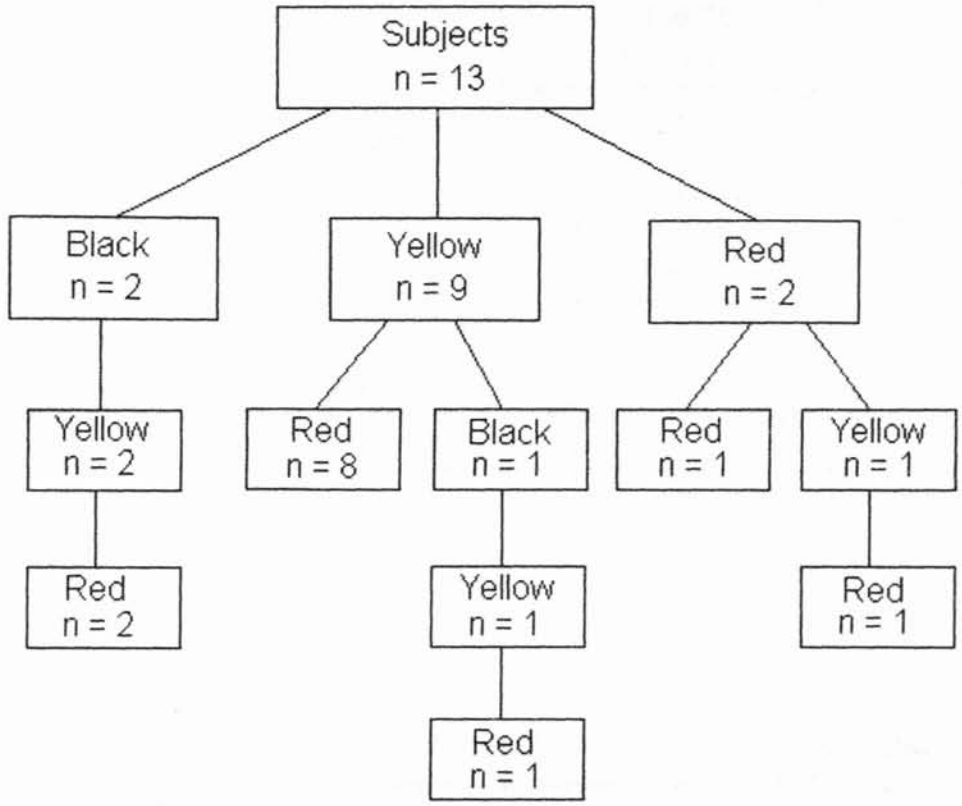

Figure 1. Systematic representation of wound healing, classified by the red-yellow-black system, in subjects who did not receive an amputation.

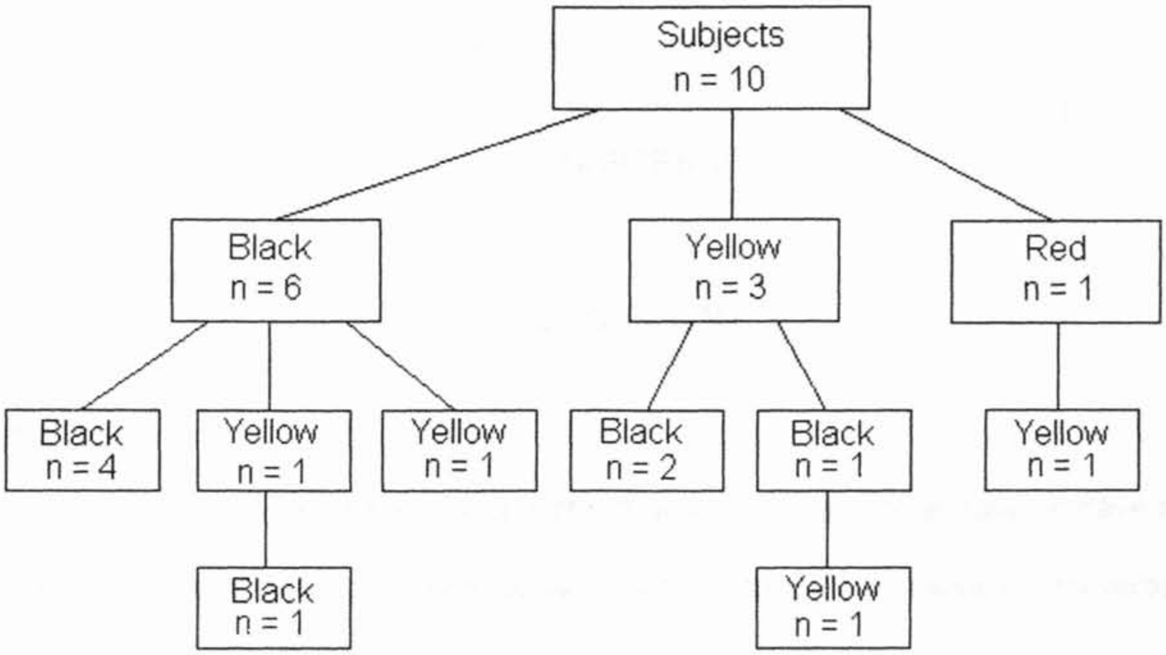

Figure 2. Systematic representation of non-healing wounds, classified by the red-yellow-black system, in subjects who received amputations.

CHAPTER V

DISCUSSION

Summary

This study was designed to determine if glucose concentrations have an effect on wound healing in subjects with diabetic foot ulcers receiving hyperbaric oxygen therapy. A retrospective review of medical charts in the baromedical unit at Integris Baptist Medical Center in Oklahoma City, Oklahoma was conducted. Data collected from the medical charts included age, sex, diagnoses, glucose values, location of ulcer, wound color stages, and if amputation occurred.

The results of the study indicated that there was no significant difference in glucose concentrations between individuals that did not receive an amputation and those that did receive an amputation. Both groups in this study had average glucose concentrations above normal range and were very similar (178.9 and 178.8 mg/dL). The blood glucose levels were taken before each hyperbaric oxygen therapy session. There are some possible reasons for elevated glucose concentrations in the subjects. The blood glucose concentrations taken may have not been fasting and hyperbaric oxygen therapy treatments were taken in the morning. Most of the subjects probably just ate breakfast before coming to the unit for treatments. This may cause elevated levels in the subjects. Another possible cause for elevated glucose concentrations is the presence of infection in the ulcer. Infection and sickness elevates glucose concentrations in individuals. Lastly, most of the individuals probably have not had good glycemic control in the past or present because the development of ulcers occur with poor glycemic control (6,9).

A study that supported relation between glycemic control and complications was the DCCT (6). The researchers studied 1441 patients with type 1 diabetes and randomly assigned them to a group. One group took part in intensive therapy to keep tight glycemic control by the use of insulin best fitting for the subject. The control group received conventional treatment. Each subject was monitored for 6.5 years and was assessed for the appearance or progression of complications that arise from diabetes. The researchers in this study observed that there was a reduction in clinical neuropathy (60%) and a reduction of peripheral vascular disease (40%) in subjects that maintained tight glycemic control compared to those in the conventional treatment group. The reduction of these complications (precursors for amputation) is a preventive measure for the incidence of amputation.

In this study, both groups had similar glucose concentrations which were above 140mg/dL. Thirteen subjects did not receive an amputation and ten subjects did. Similar glucose concentrations were observed in the groups (non-amputees and amputees) which contrary to the literture (6,9) indicated that glucose concentrations did not have an effect on the incidence of amputation.

In examining subject in this study many observations were made. One was that only fewer subjects (2 out of 13) in the non-amputated group who began HBO therapy in the black stage compared to subjects in the amputated group (6 out of 10) that started in the black stage. This leads us to surmise that the subjects that started HBO therapy at this stage were more likely to receive an amputation compared to those that started in the red or yellow stage of wound healing. Another observation was that most of the subjects were male (fifteen male and 8 female). This agrees with information in the literature review that indicated that those at high risk for the development of diabetic foot ulcers were male between the ages of 45- 64 (16). The development of diabetic foot ulcers increases with the duration of diabetes (24). The subjects in this study were in their early sixties and may have had diabetes for a long duration.

Many other complications are related to incidence and prevalence of ulcers and amputations(6, 9). A study by Moss et al. observed that good glycemic control reduces the prevalence and incidence of lower extremity amputations (9). This study included 1,210 subjects with diabetes diagnosed before the age of thirty and 1,780 subjects with diabetes diagnosed after the age of thirty. Baseline and follow-up examinations were conducted. This risk of amputation in the younger onset subjects was 9.5% and was 10.5% in the older onset subjects. Many indicators for amputation were observed in both groups. Elevated glycosylated hemoglobin concentrations was a statistically significant independent risk factor for the development of sores, ulcers and amputation.

Other risk factors discussed were long duration of diabetes, smoking, proteinuria, and low diastolic blood pressure.

This study has provided good insight to a possible future study to investigate the importance of good glycemic concentrations on wound healing of diabetic foot ulcers in subjects receiving hyperbaric oxygen therapy. As experience with this study, a retrospective review of medical chart has shown that a retrospective review of medical charts may not be a reliable source of information for the collection of data due to inconsistencies and/or the absence of information available from medical charts such as history, physicals and charting progress notes. Due to the small sample size and lack of in-depth information about the subjects, this study was limited in scope. Obtaining information from a retrospective review of medical charts presented frustrating obstacles. Exact diagnosis of type 1 or type 2 diabetes was not recorded in the medical charts. Medications or the use insulin to control diabetes were not recorded in the medical chart.

Of the 58 medical charts of patients receiving HBO for the treatment of diabetic foot ulcers, only 23 provided adequate data to be used for this study. Many charts did not have history and physical reports (76.8%), labs (92.9%) with the exception of glucose levels, completed assessments, or adequate progress notes (32.2%). Information from these components would have provided important information in understanding and analyzing the current health status of the patient. These problems could be addressed by doing a prospective study.

<u>Suggestions for a Future Study</u>

A prospective study is a better research method to determine if glycemic control has an effect on the healing of diabetic foot ulcer in subjects receiving HBO. It would provide a future investigator with measurable information to form conclusions.

A prospective study includes working closely with the other healthcare providers in a facility, providing intensive medical nutrition therapy with the patients, obtaining labs to identify the nutritional status of the individual, and keeping complete, in-depth medical charts. These interventions can provide a future investigator with needed data to provide a more conclusive study.

A future prospective study on the effect of glycemic control on wound healing in subjects receiving HBO can be more extensive and controllable. Direct communication with the subject can provide information that is not available from medical charts such as eating habits, physical activity, and feelings towards the condition. These factors can give the investigator better insight of the subject and how well they understand the importance of controlling diabetes to assist in wound healing and prevention of future complications. Understanding the subject allows for good medical nutrition therapy and education. Providing education along with other healthcare providers on the importance of maintaining good glycemic control and taking special care of the wound is beneficial for the patient.

A prospective study allows for blood to be drawn to assess the nutritional status of the subject. Good nutritional status is essential for proper wound healing. Labs such as albumin, sodium, potassium, calcium, hemoglobin and hematocrit are good indicators to use to assess the current nutritional status of the subject. It can be planned for in advance.

Assessing the glycemic control of the subject can be more reliable using hemoglobin A1c in addition to glucose concentrations. Hemoglobin A1c would provide the investigator with a good tool to measure the subjects true glycemic control over the past 6-12 weeks. Glucose concentrations give the investigator levels at only one time rather over an extended time. Hemoglobin A1c would be a more accurate measure of glycemic control.

Thorough and consistent charting and assessments (initial and throughout treatment) provides good information on the progress of the subject receiving therapy for a wound. Providing good information on the progress of wound healing includes documentation on the measurement of the wound, color of the wound, and any other changes in the subject's condition. This information should be written in progress notes and/or an assessment form.

Assessing the healing of the diabetic foot ulcer can be more reliable using measurements instead of colors. In this retrospective study, healing of foot ulcers were determined by the color of the ulcer. Very few measurements were taken throughout the treatment process. Measurements at each treatment were not available to assess the healing rate of the ulcer but the color of the wound was available. In a prospective study, good documentation of the measurements of the wounds can provide a good tool in assessing the healing rate of diabetic foot ulcers. To estimate the healing rate of the ulcers, the measurement (area) of the ulcer after the last hyperbaric oxygen therapy treatment subtracted from the measurement (area) of the ulcer before the first hyperbaric oxygen therapy treatment can be quantified and divided by the number of treatments. This will provide more definitive data on the healing rate of the wound to compare to glycemic control.

Overall, a future prospective study should include: working with a multidisciplinary staff, communication and medical nutrition therapy on the importance of glycemic control with the patient, labs to assess nutritional status, thorough assessment/ charting and measuring the wound each treatment. These elements can provide a good future study.

Many opportunities are available when doing a prospective study. Most importantly, communication with the patient allows for better understanding of the individual. This can open a door of opportunity to further educate the patient on the importance on controlling diabetes and taking good care of their health. Prospective studies can provide the opportunity for collecting important information that is otherwise not available when doing a retrospective study such as wound measurements and lab values.

Conclusions

This study was not able to clearly show the relationship of glucose concentrations and wound healing due to the small sample size and limited information regarding the subjects but provides a good beginning for a future study. This study has shown that obtaining viable data for this study requires a prospective study. Relying on medical charts of the past does not guarantee that all information that should be in the chart will be there. By doing a prospective study, with the assistance of other medical healthcare professionals, will ensure that all data required to form a valid conclusion will be available.

BIBLIOGRAPHY

1. Mayfield J, Reiber G, Sanders L, Janisse D, Pogach L. Preventive foot care in people with diabetes. *Diabetes Care* 21(12):, 1999
2. Cianci P. Adjunctive hyperbaric oxygen therapy in the treatment of the diabetic foot. *J Am Pod Med Assoc* 84(9): 448-455, 1994
3. Centers for Disease Control and Prevention, 1996. Available from www.cdc.gov/health/diabetes/htm. Accessed 20 January 2001
4. Lavery LA, Armstrong DG, Harkless LB. Classification of diabetic foot wounds. *J Foot Ankle Surg* 35(6): 528-531, 1996
5. Sussman K, Draznin B, James W (Eds). *Clinical Guide to Diabetes Mellitus.* New York, Alan R Liss, Inc., 1987
6. Diabetes Control and Complication Trial Research Group:The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin dependent diabetes mellitus. *N Eng J Med* 329: 977-986, 1993
7. Litzelman DK, Slemenda CW, Langfeld CD, Hays LM, Welch MA, Bild ME, Ford ES, Vinicor EF: Reduction of lower extremity clinical abnormalities in patients with non-insulin dependent diabetes mellitus. *Ann Intern Med* 119: 36-41, 1993

8. Faglia E, Oriani G, Favales F, Michael M, Aldeghi A, Campagnoli P, Calia P, Morabito A, Quarantiello A. Adjunctive systemic hyperbaric oxygen therapy in treatment of severe prevalently ischemic diabetic foot ulcer. *Diabetes Care* 19: 1338-1343, 1995

9. Moss SE, Klein R, Klein BEK: The prevalence and incidence of lower extremity amputation in diabetic population. *Arch Intern Med* 153: 610-616, 1992

10. National Institute of Diabetes and Digestive and Kidney Diseases, 2001. Available from www.niddk.nih.gov/health/diabetes/pubs/dmover/dmover.htm. Accessed 20 January 2001

11. American Diabetes Association, 2002. Available from www.americandiebetesassociation.org. Accessed 08 April 2002

12. Report of the expert committee on the diagnosis and classification of diabetes mellitus. The expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 25(1): S5-S16, 2002

13. Wildman R, Medeiros D. *Advanced Human Nutrition.* New York, CRC Press, 2000

14. US Renal Data System: *USRDS 1998 Report.* Bethesda, MD, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 1998

15. Reiber GE, Boyko EJ, Smith DG: Lower extremity foot ulcers and amputations in diabetes. In *Diabetes in America.* 2nd ed. Harris Me,

Cowie CC, Reiber GE, Boylo EJ, Stern M, Bennett P, Eds. National Institutes of Health. NIH Publication No. 95-1468, 1995

16. Klein R, Klein B. Relation of glycemic control to diabetic complications and health outcomes. *Diabetes Care* 21(3), 1998

17. Consensus Development Conference on Diabetic Foot Wound Care: American Diabetes Association. *Diabetes Care* 22: 1354-1360, 1999

18. Miller BF, Keane CB. *Encyclopedia and Dictionary of Medicine, Nursing and Allied Health.* 4th ed. Philadelphia, WB Saunders Co, 1987

19. Armstrong DG, Lavery LA. *American Family Physician* . Available from www.aafp.org/afp/980315ap/arstron.html. Assessed on 24 March 2002

20. Lysen, LK: *Quick Reference to Clinical Dietetics.* Gaithersburg, Maryland, Aspen Publications Inc., 1997

21. Krasner D. Wound Care: How to use the red-yellow-black system. *Am J Nurs* May 44-47, 1995

22. Harris M, Eastman R, Cowie C. Symptoms of sensory neuropathy in adults with NIDDM in the US population. *Diabetes Care* 16: 1146-1452, 1993

23. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, Wilson DM. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population based cohort: the Rochester Diabetic Neuropathy Study. *Neurology* 43:817-824, 1993

24. Paulumbo PJ, Melton LJ: Peripheral vascular disease and diabetes. In *Diabetes in America* 2nd ed. Harris ME, Cowie CC, Reiber G, Boyko E,

Stern M, Bennett P, Eds. National Institutes of Health, NIH Publication No. 95-1468, 1995

25. Kannell WB, McGee DL. Diabetes and cardiovascular disease: the Frammingham Study. *JAMA* 241:2035-2038, 1979

26. Apelqvist J, Larsson J, Agardh CD. The influence of external precipitating factors and peripheral neuropathy on the development and outcome of diabetic foot ulcers. *J Diabetes Complications* 4: 21-25, 1990

27. Pecoraro RE, Reiber GE, Burgess EM. Pathways of diabetic limb amputation: basis for prevention. *Diabetes Care* 13: 513-521, 1990

28. Wyss CR, Harrington RM, Butgess EM, Matsen RA. Transcutaneous oxygen tension as a predictor of success after an amputation. *J Bone Joint Surg* 70: 203-207, 1988

29. Hunt TK. The physiology of wound healing. *Ann of Emerg Med* 17: 1265-1273, 1988

30. Hoogwerf BJ. Postoperative management of the diabetic patient. *Med Clin North Am* 85(5): 1213-1228, 2001

31. Rojas A, Phillips T. Patients with chronic leg ulcers show diminished levels of Vitamins A and E, carotenes, and zinc. *Dermatologic Surgery* 25(8): 601-604, 1999

32. U.S. Department of Health and Human Services. *Treatment of Pressure Ulcers.* AHCPR Publication No. 95-0652, December 1994

33. Bello Y, Phillips T. Recent advances in wound healing. *JAMA* 28: 716, 2000

34. Tovey FI. The manufacture of diabetic footwear. *Diabet Med* 1: 69-71, 1984

35. Gibbons GW, Burgess AM, Guadgnoli E, Pomposelli FB, Freeman DV, Campbell DR, Miller A, Marcaccio EJ, Nordberg P, LoFerfo FW. Return to well-being and function after infrainguinal revascularization. *J Vasc Surg* 21: 35-45, 1995

36. Leach RM, Rees PJ, Wilmshurst P. ABCs of oxygen: Hyperbaric oxygen therapy. *Br Med J* 317: 1140-1143, 1998

37. Kindwall E, Ed. *Hyperbaric Medicine Practice.* Flagstaff, AZ, Best Publishing Company, 1995

38. Young, T. Hyperbaric oxygen therapy in wound management. *Br J Nurs* 4: 796-803, 1995

39. Cianci P, Sato R. Adjunctive hyperbaric oxygen therapy in the treatment of thermal burns: a review. *Burns* 20: 5-14, 1994

40. Tabrah FL, Tanner R, Vega R, Batkin S. Baromedicine today- Rational uses of hyperbaric oxygen therapy. *Hawaii Med J* 53: 112-119, 1994

41. Hunt TK, Hopf HW. Wound healing and wound infection: what surgeons and anesthesilogists can do. *Surg Clin North Am* 77(3): 587-606, 1997

42. Baroni G, Porro T, Faglia E. Hyperbaric oxygen in diabetic gangrene treatment. *Diabetes Care* 10: 81, 1987

APPENDICES

APPENDIX A

APPENDIX B

Oklahoma State University
Institutional Review Board

Protocol Expires: 9/16/02

Date: Monday, September 17, 2001 IRB Application No HE0214

Proposal Title: THE EFFECT OF GLYCEMIC CONTROL ON THE HEALING RATES OF DIABETIC FOOT ULCERS IN SUBJECTS RECEIVING HYPERBARIC OXYGEN THERAPY

Principal Investigator(s):

Kathryn Brown	Maria Spicer
1823 N. Dobi Lane	425 HES
Stillwater, OK 74075	Stillwater, OK 74078

Reviewed and Processed as: Expedited

Approval Status Recommended by Reviewer(s): Approved

Dear PI :

Your IRB application referenced above has been approved for one calendar year. Please make note of the expiration date indicated above. It is the judgment of the reviewers that the rights and welfare of individuals who may be asked to participate in this study will be respected, and that the research will be conducted in a manner consistent with the IRB requirements as outlined in section 45 CFR 46.

As Principal Investigator, it is your responsibility to do the following:

1. Conduct this study exactly as it has been approved. Any modifications to the research protocol must be submitted with the appropriate signatures for IRB approval.
2. Submit a request for continuation if the study extends beyond the approval period of one calendar year. This continuation must receive IRB review and approval before the research can continue.
3. Report any adverse events to the IRB Chair promptly. Adverse events are those which are unanticipated and impact the subjects during the course of this research; and
4. Notify the IRB office in writing when your research project is complete.

Please note that approved projects are subject to monitoring by the IRB. If you have questions about the IRB procedures or need any assistance from the Board, please contact Sharon Bacher, the Executive Secretary to the IRB, in 203 Whitehurst (phone: 405-744-5700, sbacher@okstate.edu).

Sincerely,

Carol Olson

Carol Olson, Chair
Institutional Review Board

APPENDIX C

April 6, 2001

R.C. Brown, M.D.
Institutional Review Board
3300 Northwest Expressway
Oklahoma City, OK 73112

Dear Doctor Brown:

Please review the following protocol for the Institutional Review Board. This protocol is for Expedited Review, which means the **protocol involves non-significant risk.** The protocol requires only the review and signature of a designated committee member and not a full committee review.

If you have any questions or concerns, please feel free to contact me at my office at (405) 707-9507.

Sincerely,

Katherine Mannin/ds

Katherine Mannin
Principal Investigator

Protocol Title: **The Effect of Glycemic Control on the Healing Rates of Diabetic Foot Ulcers in Subjects Receiving Hyperbaric Oxygen Therapy (Z0103173)**

Requested Change: **Approval of protocol**

Is Protocol Change approved? YES ____________
NO ____________ (need more information to complete review.)

____________________ SIGNATURE OF IRB CHAIRMAN

4/6/01
DATE

APPENDIX D

Patient number:_______

Age/ Sex:________
Diagnosis:____

Location of ulcer:____

Initial Tx & Color:____

Black

Date changed black	Glucose Range	Glucose Average	Number of treatments

Yellow

Date changed yellow	Glucose Range	Glucose Average	Number of treatments

Red

Date changed red	Glucose Range	Glucose Average	Number of treatments

Patient number:_______

Age/ Sex:________
Diagnosis:____

Location of ulcer:____

Initial Tx & Color:____

Black

Date changed black	Glucose Range	Glucose Average	Number of treatments

Yellow

Date changed yellow	Glucose Range	Glucose Average	Number of treatments

Red

Date changed red	Glucose Range	Glucose Average	Number of treatments

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VITA

Kathryn Michelle Brown

Candidate for the Degree of

Master of Science

Thesis: THE EFFECT OF GLUCOSE CONCENTRATIONS ON THE HEALING OF DIABETIC FOOT ULCERS IN SUBJECTS RECEIVING HYPERBARIC OXYGEN THERAPY

Major Field: Nutritional Sciences

Biographical:

Personal Data: Born in Sacramento, California, on May 16, 1976, the daughter of Owen and Stephanie Mannin

Education: Graduated from Westmoore High School, Oklahoma City, Oklahoma in May 1994; received Bachelor of Science degree in Dietetics from Oklahoma State University, Stillwater, Oklahoma in December 1998. Completed the requirements for the Master of Science degree in Nutritional Sciences from Oklahoma State University, Stillwater, Oklahoma in May 2002.

Professional Memberships: American Dietetic Association, Oklahoma Dietetic Association, Phi Kappa Phi